Endovascular radiofrequency ablation: A novel treatment of venous insufficiency in Klippel-Trenaunay patients

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Introduction: **Klippel-Trenaunay Syndrome (KTS) is an uncommon congenital disorder of uncertain etiology that comprises the clinical triad of varicose veins, port wine stain, and bony or soft-tissue hypertrophy. The literature suggests that the deep venous system is often under-developed. We propose that duplex venous ultrasound can effectively demonstrate patent deep venous systems in KTS patients with mild to moderate disease, and that endovascular radiofrequency ablation can be utilized in a safe and appropriate therapeutic manner.**

Methods: **A single center retrospective review of three patients with KTS treated with endovascular radiofrequency ablation of the KT veins and/or great saphenous veins was conducted. Preoperatively, patients underwent both venography and were studied with color flow duplex ultrasound system iU22 with a 7-5 MHz linear array probe (Philips Medical Systems, NA, Bothell, Wash). The anomalous KT veins, great saphenous and saphenous tributaries, and associated incompetent perforators were ablated with radiofrequency catheters (VNUS Medical Technologies, Inc, San Jose, Calif). All the radiofrequency ablations were complimented by ultrasound guided sclerotherapy of the varicose tributaries and when evident, incompetent perforator veins.**

Results: **The diagnostic series of duplex ultrasounds performed on our KTS patients has demonstrated contiguous deep venous systems in the effected extremity and effectively recognized the associated anomalous superficial venous systems. Our treatment resulted in successful occlusion of the incompetent veins in all three patients.**

Discussion: **The three patients, females aged 39, 19, and 16, presented with port wine stains and many years of leg-swelling and varicose veins that were recalcitrant to conservative treatment measures, including compression stockings and pulsed-dye laser therapy. Venography initially revealed poorly developed deep venous systems. However, venous ultrasound demonstrated patent and competent deep venous systems in all of the affected limbs. Radiofrequency ablations were performed to manage the sequella of venous insufficiency. At short-term follow-up, all patients demonstrated markedly decreased leg pain, edema, and varicose vein bulging.**

Conclusions: **Three KTS patients were successfully treated with radiofrequency ablation of the incompetent great saphenous and/or anomalous superficial veins. Although the deep veins were poorly visualized on venography, they were clearly demonstrated with duplex ultrasound and functioned adequately once the incompetent superficial veins were ablated. (J Vasc Surg 2008;47:1339-45.)**

First reported in the literature in 1900, Klippel-Trenaunay syndrome (KTS) triad classically consists of tissue hypertrophy, varicose veins, and port wine stain.[1] In an estimated 95% of patients, the extremities are involved. The majority of KTS patients exhibit venous anomalies such as persistent sciatic vein and enlarged lateral veins.[2,3] The symptoms can be of varying degrees ranging from minimal in which patients only have a capillary hemangioma or varicose veins to the extreme in which there is a gross deformity in the limb resulting in disability (Fig 1).

Sonography, contrast venography, and magnetic resonance (MR) angiography constitute the typical diagnostic workup for evaluating the vascular status.[4-6] A study by Howlett et al in 1994 determined Doppler ultrasound to be more reliable than venography.[7] Indeed, the use of sonography has demonstrated patent deep venous systems in the majority of KTS patients.[7] MR angiography is also beginning to supplant venography in treatment planning,[6] especially on those patients who present with unclassified venous and arteriovenous malformations. Recently, three-dimensional (3D) MR venography and multidetector computed tomography (CT) have been shown to yield useful information concerning both the status of the soft-tissue and venous systems.[8] In our experience, the delineation of venous anatomy offered with duplex ultrasound is more complete than with standard venography.

Treatment of KTS patients has consisted mainly of conservative medical management, including compressive stockings and anti-inflammatory medications for pain relief. Operative treatment has been controversial and surgery on the superficial venous system has been reserved for patients with intact deep systems only. However, Servelle reported satisfactory results from release of fibrous bands on the deep veins when compression was evident.[9] Limited varicose vein excision can improve focal symptoms in most KTS

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Fig 1. Klippel Trenaunay syndrome.

patients but recurrence and worsening of symptoms occurred in a few of these patients.[2,10,11] Baraldini et al proposed early surgical intervention in order to prevent further complications of KTS.[12] Ultrasound-guided sclerosant foam therapy in KTS patients is minimally-invasive and yields promising results with few complications, although the procedure must be repeated numerous times.[13] We think that this may be risky in potentially high-flow venous channels of large diameter.

In this study, we present a limited clinical experience of an aggressive approach to the treatment of superficial venous varices utilizing endovenous thermal ablation via radiofrequency (RFA) complimented by ultrasound guided sclerotherapy in KTS patients as a minimally invasive and potentially efficacious treatment.

METHODS

A single center retrospective review of three KTS patients treated with RFA of the KT veins and/or the great saphenous veins was conducted. Preoperatively, patients were studied with color flow duplex ultrasound system iU22 with a 7-5 MHz linear array probe (Philips Medical Systems, NA, Bothell, Wash) and venography. Patients in our KTS population were tested in a supine position with reverse Trendelenberg of $\simeq$ 30%. Limb positioning is determined by the vessels being evaluated. Determining deep venous patency is dependant on basic examination protocols for ruling out venous obstruction. This includes compression maneuvers and both color and spectral Doppler analysis.

The anomalous KT veins, great saphenous and associated tributaries, as well as incompetent perforator veins were ablated with radiofrequency catheters (VNUS Medical Technologies, Inc, San Jose, Calif). The RFA procedure utilizes tumescent solution consisting of 400 cc of normal saline, 4 cc of 8.4% sodium bicarbonate and 40 cc of 1% lidocaine. Tumescence was then infused around the saphenous vein deep to the subfascia or in the subcutaneous space for the anomalous KT veins. Attempt was made to inject adequate tumescent to achieve a vein depth of $\geq$1 cm. Once 1% lidocaine had been injected, the anomalous veins were cannulated with the RFA catheter. Treatment was temperature controlled and begun at 85 to 90 degrees Celsius using a 6F catheter (RFAc), withdrawing at a rate of 2 to 3 cm per minute. Temperature controlled treatment of 120 Celsius when using a 7F catheter (RFAf) and treating 7cm segments for 20 seconds. Concomitant 3% sotradecol was injected into the varicose tributaries of the ablated vein in order to reduce flow impending on the treated segments. Patients were sent home the same day wearing 20 to 30 mm Hg compression stockings. Repeated sclerotherapy was often required. Additional follow-up also consisted of venous duplex ultrasonography to evaluate the presence of deep system patency and continued ablation of the superficial system. Ultrasounds were scheduled 4 days post ablation, at 1 month and then every 1 to 2 months for approximately 26 weeks. Contrast venography performed prior to the ultrasound was with the modified Rabinov technique that evaluates the patient in a supine position with and without tourniquet.

RESULTS

In all three patients, the deep venous system was thought to be absent or poorly developed with standard venography techniques. Initial contrast venography revealed only saphenous and superficial varicosity filling with no evidence of the deep system patency (Fig 2). However, venography repeated with ankle tourniquet revealed filling of the popliteal and femoral veins though the filling was minimal and inconsistent. The radiological impression was of a typically underdeveloped or hypotrophic deep venous system (Fig 3, *A* and *B*). Deep venous filling was also absent on one venogram that was performed elsewhere though we are unsure of the technique used. Venous duplex imaging of the affected lower extremities in each of the patients demonstrated intact deep venous systems without evidence of obstruction. There was mild deep venous insufficiency noted in two of the three patients prior to the procedure. The deep veins appeared to be otherwise normal in function and size and not hypotrophic (Fig 4, *A* and *B*). Superficial reflux was demonstrated either through the saphenous or the anomalous superficial veins in the extremity. In addition, dilated incompetent perforator vessels were observed communicating laterally with the KT vein around the knee and in the calf in the patients with this anomalous vein and with the posterior arch vein in the patient with the incompetent great saphenous vein. Vessel diameters ranged from 5 mm to 15 mm.

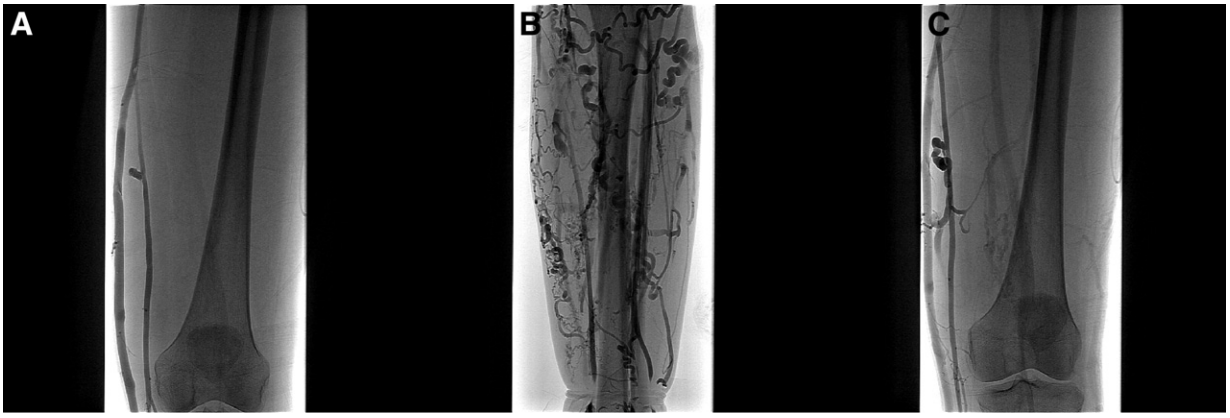

Fig 2. A, Hypotrophic deep veins in thigh. **B,** Hypotrophic deep veins with anomalous superficial veins in calf. **C,** Deep veins visualized with thigh tourniquet.

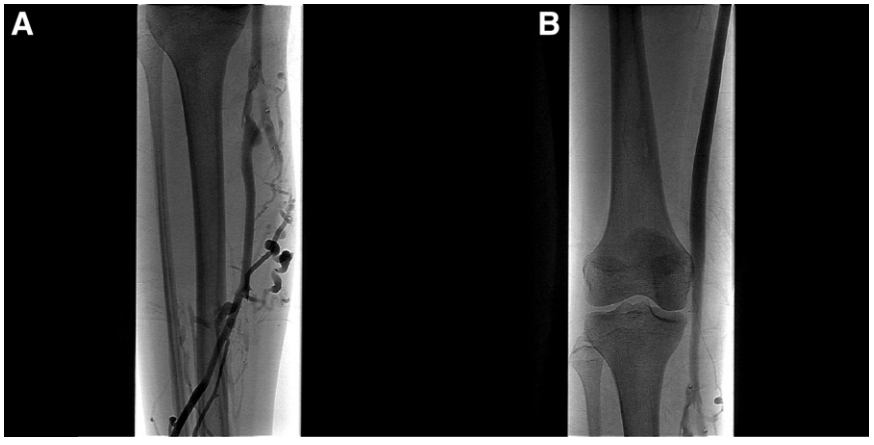

Fig 3. A, Venogram of hypertrophic superficial system with absence of deep venous system. **B,** Venogram showing only superficial outflow in the leg.

The endovenous thermal ablation was generally well-tolerated by all the patients. However, one patient experienced burning pain at the onset of the RFA that required premature cessation of the treatment in the affected area. This was thought to be due to inadequate tumescence.

Duplex venous ultrasound performed at completion of the procedures confirmed thickening of the vessel walls with apparent occlusion of the Klippel-Trenaunay or saphenous veins in each of the patients (Fig 5).

The degree of varicose vein bulging, pain, and swelling improved noticeably and immediately following the procedure in two of the patients and noticed by the third patient after undergoing a second ablation to noticeably reduce the luminal diameter. Indeed, one patient described her toes as "appearing longer" after the procedure as the result of the diminished edema. However, the procedures were not without complications. One patient developed asymptomatic propagation of thrombus into the posterior tibial vein resulting in an isolated deep vein thrombosis at the site of RFA of an incompetent perforator vein (RFS). One patient experienced a cutaneous ulceration in the thigh at the site of reported burning sensation. The procedure was stopped immediately and concomitant sclerosing of the patent segments of the vessel and the adjacent superficial and perforating veins was performed. This vessel reopened several months after the procedure. This occurred even with multiple sessions of sclerosing. The vessel was re-ablated with radiofrequency along with the communicating anterior branch to the saphenous and the great saphenous vein in the thigh. The vessel is currently closed with improvement of the patients' symptoms and appearance (Fig 6, *A* and *B*).

One patient required multiple thermal ablations including a laser treatment with (Diomed EVLT laser, Diomed Holdings, Inc, Andover, Mass), when the initial ablation failed to adequately treat the vessel (Table). This treatment also failed most likely due to large diameter of the vessel 15 mm and patent varicose tributaries supplying flow to the treated segment.

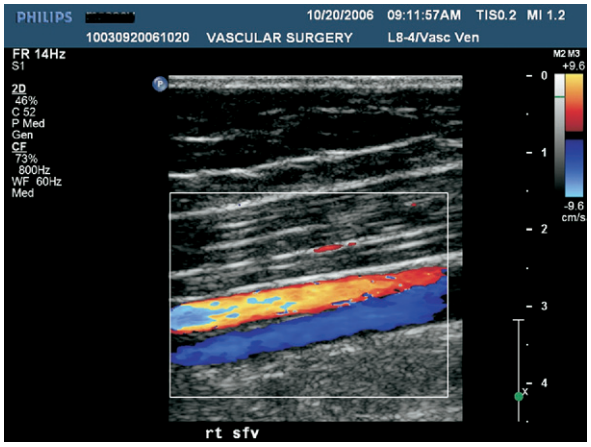

Fig 4. Color duplex image of patent deep venous system.

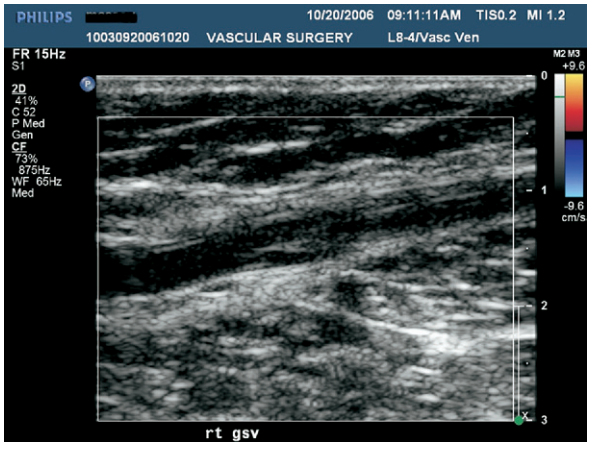

Fig 5. Great saphenous vein closed after thermal ablation.

DISCUSSION

This retrospective study comprised of three female patients, aged 38, 19, and 16 years at the time of the intervention. All three patients experienced pain and swelling of the affected extremity with exertion or standing for long periods. All three suffered from gross varicosities and port wine stain. Additional complaints included a macular cutaneous component and angiokeratomas that occasionally bleed, a sizable venous malformation in the extremity, and soft and bony tissue hypertrophy with orthopedic disturbances that developed in early childhood.

Our observation that duplex venous ultrasound enables detection of intact deep venous systems in the patients with KTS concurs with previous reports of this phenomenon; however, this is not widely appreciated and for good reason. Occasionally, the deep system will be absent. Placing the patient in a supine position and using a duplex protocol that incorporates color flow mapping is very helpful due to the presence of tissue hypertrophy and edema. Recognizing the spontaneity of the venous flow with respiration is also important in these patients because adequate distal augmentations

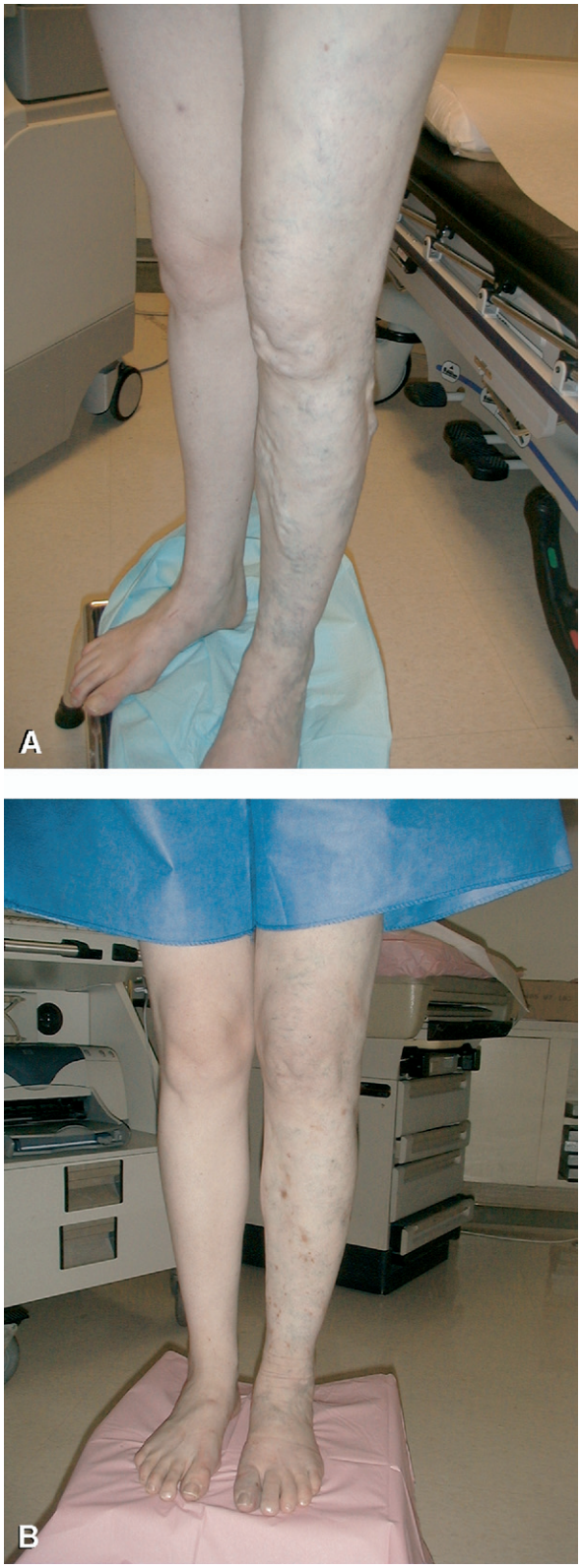

Fig 6. A, Preop edema, varicosities, and limb hypertrophy. **B,** Decrease in gross varicosities, ankle and foot swelling s/p thermal ablation.

Table. Summary of treatments

PT	*RFA device*	*Target vessel GSV*	*Additional target vessel*	*RFAs perfs*	*ReDo RFA*	*Concomit sclero u/s guide*
1	RFAc	GSV	—	X2 prox mid calf	no	GSV tribs Calf perfs
2	RFAf	GSV	KT branch anterior thigh-GSV		EVLT RFAf (x2)	KT tribs To GSV KT vein @ venous malformation
3	RFAc	KTV		Lateral calf	RFAf	KT vein and tribs Calf perfs

PT, Patient; *RFAc,* radiofrequency ablation closure device; *RFAf,* radiofrequency ablation fast device; *RFS,* radiofrequency ablation perforator veins; *EVLT,* laser ablation; *KTS,* Klippel-Trenaunay syndrome; *GSV,* great saphenous vein.

may not be appreciated due to both physical constraints and the dramatically increased venous hypertension in standing KTS patients. Venous insufficiency is readily apparent in the anomalous superficial system regardless of positioning. Thus, our experience with venography as providing inconclusive assessment of the deep venous systems supports the claim by Howlett[7] that sonography can be a superior modality for this purpose. Nevertheless, ultrasound interrogation of the deep system in these patients can be quite challenging. The ultrasound evaluations are much more complex than routine studies typically performed for deep venous thrombosis. The technologist must have a familiarity with gross anatomy of the thigh and calf, a thorough knowledge of venous representation by duplex ultrasound, and good comprehension of venous hemodynamics to assess functional obstruction. Only after complete venographic and ultrasonic evaluation in these three very symptomatic young women did we propose occluding the incompetent superficial venous systems.

There are several advantages for using radiofrequency ablation of incompetent superficial veins. It has been clearly shown to be a cost-effective alternative to vein stripping and ligation.[14] In addition, the minimally invasive nature of the procedure reduces bleeding and wound complications. This is of even greater benefit when dealing with patients with venous malformations where one would expect bleeding to be significantly increased. The technique has been proven to be durable. Merchant et al reported greater than 80% occlusion rates in saphenous veins in a long-term trial of non-KTS patients.[15] RFA can be used successfully in KTS patients as long as one is certain of the deep and superficial venous anatomy. RFA of the incompetent veins in our KTS patients was performed only as a result of the recognition of a patent deep venous system by duplex ultrasound. An intact deep venous system is an essential criterion that must be established prior to pursuing aggressive therapies, to avoid serious consequences. On the other hand, relying solely on contrast venography to determine the presence of a contiguous deep venous system may unfairly restrict the symptomatic patient population from participating in these minimally invasive therapies. We felt confident based on our duplex ultrasound evaluation to treat these patients in spite of poor correlative evidence provided by venography where the deep veins appeared hypoplastic even in the presence of a tourniquet.

The complications that arose in our patient group from this thermal ablation were either potentially avoidable or amendable. The isolated thrombosis of the posterior tibial vein propagated from a thermal ablation of the perforator vein would have been avoided by not performing that procedure if we would have known what a subsequent coagulation profile demonstrated a lupus inhibitor and increased antiphospholipid antibodies revealing a significantly thrombophilic patient. Follow-up ultrasound showed thrombus resolution with complete recanalization of the vessel. The burning pain and subsequent cutaneous ulceration secondary to skin burn was attributed to insufficient tumescent solution in an isolated segment of a very superficial vein. This was not a problem with other superficial veins where adequate tumescence was used. The untoward occurrence of the cutaneous ulceration was also potentially complicated by our concomitant use of a sclerosant agent to the affected area. With the cessation of radiofrequency upon complaints of a burning sensation, we injected 3% solution of sclerosing agent into the vein to increase to probability of vein occlusion. Min and Khilnani report that a potential cause for the skin injury is the use of foam sclerotherapy immediately following endovenous ablation due to the possibility of extravasation of sclerosant related to tumescent anesthesia administration.[20] Other complications reported with endovenous ablation of the saphenous vein include bruising, cutaneous paresthesias, deep vein thrombosis, and skin burns.[16] To date, skin burn rates ranging from 0% to 20% have been reported with RFA.[17-19]

The incomplete occlusion of the incompetent great saphenous vein in the patient with multiple thermal ablations is likely due to the overwhelmingly large great saphenous vein (15 mm diameter preoperatively) and the presence of large patent varicose tributaries promoting flow into the vessel. Indeed, reports describe that nonocclusion is associated with technical failures attributed to large vein diameter, while recurrence appears to be a result of anatomical failures such as remaining untreated collateral veins or "feeding" varicosities that contribute to the recanalization.[15,21] These factors may partly result from the progressive nature of this disease, and we expect recanalization to occur more frequently in this patient population. This is why we often perform concomitant and subsequent sclerotherapy of these venous tributaries. Continued surveillance is required and adjunctive therapies such as sclerotherapy and additional thermal ablations may be necessary to combat the progression of venous insufficiency. The patient's symptoms are improved and remain stable at four month follow-up (Fig 7, *A* and *B*).

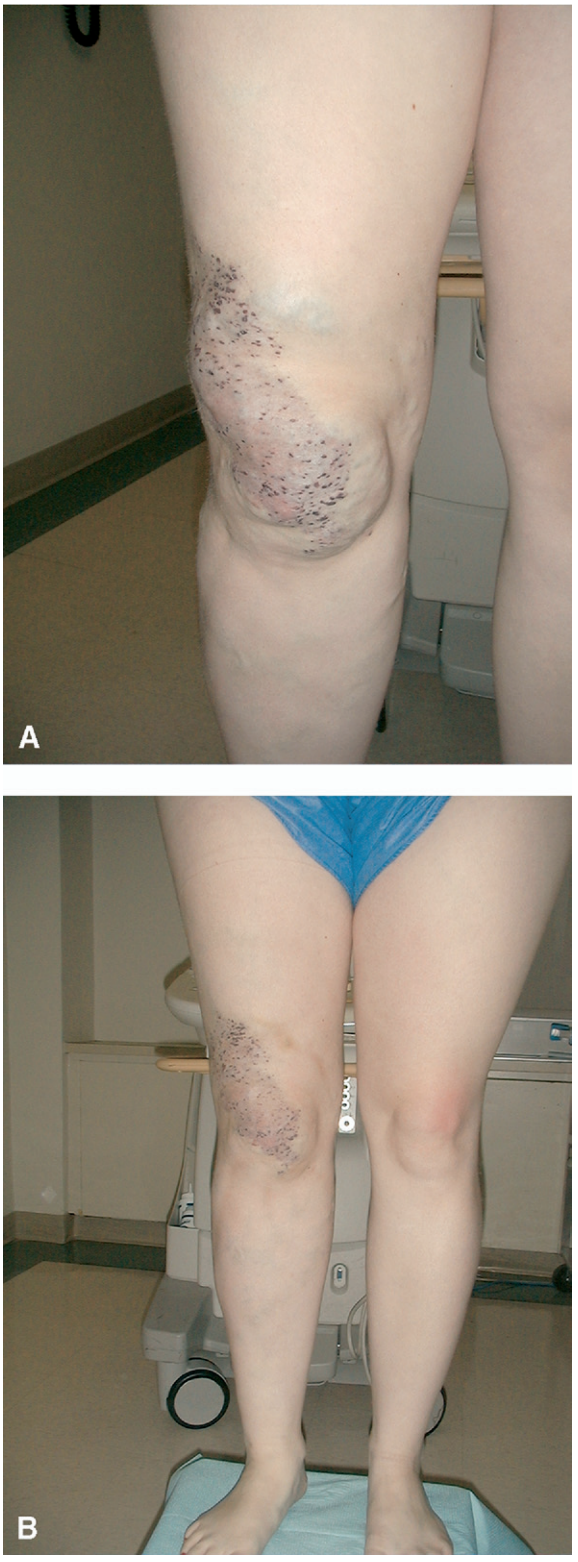

Fig 7. A, Preop varicosities and venous malformation. **B,** Postop with decrease in varicosities and malformation sensitivity. However, segments of the great saphenous vein and Klippel-Trenaunay tributaries remain open.

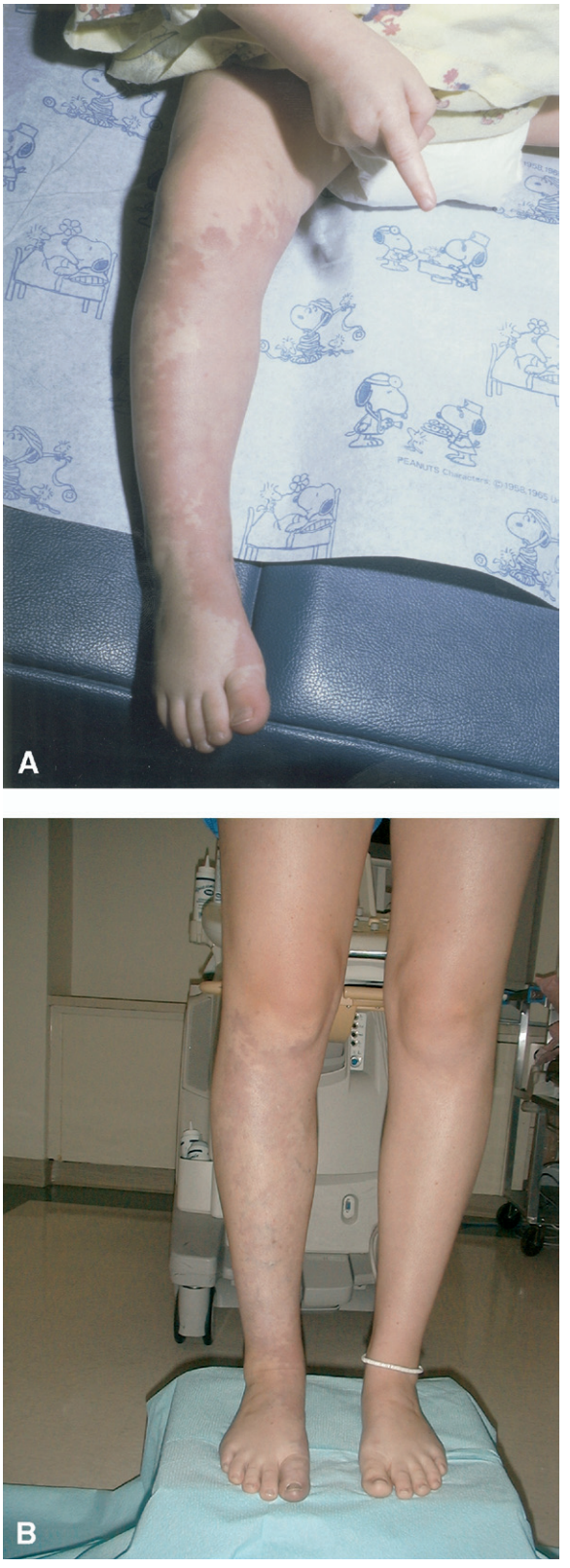

Fig 8. A, Klippel-Trenaunay Syndrome in infancy. **B,** Ten months s/p thermal ablation.

CONCLUSIONS

Although deep veins in three KTS patients were poorly visualized on venography, they were clearly demonstrated on duplex ultrasound and became functional once the incompetent superficial veins were ablated. Indeed, chronic edema and discomfort were dramatically alleviated with ultrasound-guided radiofrequency ablation of the KT and/or great saphenous veins. This notwithstanding, prior to attempting closure of the incompetent veins, detailed duplex ultrasonography must adequately characterize the affected vessels and visualize a patent deep venous system.

Thermal ablation is a minimally invasive alternative to painful vein stripping surgery that can be performed as an ambulatory procedure. It is a particularly attractive option with this patient population. However, these patients need continued follow-up, and one should anticipate the need for continued sclerotherapy and/or thermal ablation treatments if veins recanalize (Fig 8, *A* and *B*). From our limited experience, we have seen a greater need for continued close monitoring after treatment because two of the three patients required retreatment. While radiofrequency ablation appears to provide satisfactory cosmetic results and relief from pain and swelling in short-term follow-up, a larger patient volume in carefully selected patients over longer periods is warranted.

REFERENCES

1. Klippel M, Tranaunay P. Du noevus variquex oste-hypertrophic. Arch Gen Med (Paris) 1900;185:641-72.
2. Jacob AG, Driscoll DJ, Shaughnessy WJ, Stanson AW, Clay RP, Gloviczki P. Klippel-Trenaunay syndrome: spectrum and management. Mayo Clin Proc 1998;73:28-36.
3. Baskerville PA, Ackroyd JS, Lea Thomas M, Browse NL. The Klippel-Trenaunay syndrome: clinical, radiological and hemodynamic features and management. Br J Surg 1985;72:232-6.
4. Phillips GN, Gordon DH, Martin EC, Haller JO, Casarella W. The Klippel-Trenaunay syndrome: clinical and radiological aspects. Radiology 1978;128:429-34.
5. Fontana A, Olivetti L. Peripheral MR angiography of Klippel-Trenaunay syndrome. Cardiovasc Interv Radiol 2004;27:297-9.
6. Kanterman RY, Witt PD, Hsieh PS, Picus D. Klippel-Trenaunay syndrome: imaging findings and percutaneous intervention. AJR Am J Roentgenol 1996;167:989-95.
7. Howlett DC, Roebuck DJ, Frazer CK, Ayers B. The use of ultrasound in the venous assessment of lower limb Klippel-Trenaunay syndrome. Eur J Radiol 1994;18:224-6.
8. Bastarrika G, Redondo P, Sierra A, Cano D, Martínez-Cuesta A, López-Gutiérrez JC, Cabrera. New techniques for the evaluation and therapeutic planning of patients with Klippel-Trénaunay syndrome. J Am Acad Dermatol 2007;56:242-9.
9. Servelle M. Klippel and Trenaunay's syndrome. 768 operated cases. Ann Surg 1985;201:365-73.
10. Noel AA, Gloviczki P, Cherry KJ Jr, Rooke TW, Stanson AW, Driscoll DJ. Surgical treatment of venous malformations in Klippel-Trenaunay syndrome. J Vasc Surg 2000;32:840-7.
11. Gloviczki P, Stanson AW, Stickler GB, Johnson CM, Toomey BJ, Meland B, et al. Klippel-Trenaunay syndrome: the risks and benefits of vascular interventions. Surgery 1991;110:469-79.
12. Baraldini V, Coletti M, Cipolat L, Santuari D, Vercellio G. Early surgical management of Klippel-Trenaunay syndrome in childhood can prevent long-term hemodynamic effects of distal venous hypertension. J Pediatr Surg 2002;37:232-5.
13. Nitecki S, Bass A. Ultrasound-guided foam sclerotherapy in patients with Klippel-Trenaunay syndrome. Isr Med Assoc J 2007;9:72-5.
14. Rautio T, Ohinmaa A, Perälä J, Ohtonen P, Heikkinen T, Wiik H, et al. Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs. J Vasc Surg 2002;35:958-65.
15. Merchant RF, Pichot O; Closure Study Group. Long-term outcomes of endovenous radiofrequency obliteration of saphenous reflux as a treatment for superficial venous insufficiency. J Vasc Surg 2005;42:502-9; discussion 509.
16. Min RJ, Khilnani NM. Cutaneous thermal injury after endovenous laser ablation of the great saphenous vein. J Vasc Interv Radiol 2005;16:564.
17. Sichlau MJ, Ryu RK. Cutaneous thermal injury after endovenous laser ablation of the great saphenous vein. J Vasc Interv Radiol 2004;15:865-7.
18. Kabnick LS, Merchant RF. Twelve and twenty-four month follow-up after endovascular obliteration of saphenous vein reflux. A report from the multicenter registry. J Phlebol 2001;1:17-24.
19. Min RJ, Khilnani N, Zimmet S. Endovenous laser treatment of saphenous vein reflux: long-term results. J Vasc Interv Radiol 2003;14:991-6.
20. Weiss RA, Weiss MA. Controlled radiofrequency endovenous occlusion using a unique radiofrequency catheter under duplex guidance to eliminate saphenous varicose vein reflux: a 2-year follow-up. Dermatol Surg 2002;28:38-42.
21. Bauer J, Prevalence and mechanisms of failure following endovenous thermal ablation of varicose veins. J Vasc Interv Radiol 2006;17:597-748.

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